Dkt. 56376/JPW/ADM

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Douglas A. Craig

U.S. Serial No.: 09/450,880 Examiner: S. Houtteman

Filed : November 29, 1999 Group Art Unit: 1656

For : USE OF COMPOUNDS WHICH ACTIVATE A 5-HT RECEPTOR TO TREAT URINARY INCONTINENCE

1185 Avenue of the Americas
New York, New York 10036
October 11, 2001

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

AMENDMENT IN RESPONSE TO APRIL 11, 2001 OFFICE ACTION AND PETITION FOR A THREE MONTH EXTENSION OF TIME

This Amendment is submitted in response to the Office Action issued April 11, 2001 in connection with the above-identified application. A response to the April 11, 2001 Office Action was due July 11, 2001. Applicant herewith petitions for a three month extension of time in which to respond to the April 11, 2001 Office Action. The fee for a three month extension is NINE HUNDRED TWENTY DOLLARS ($920.00) and a check in this amount is enclosed. With a three month extension of time, a response to the April 11, 2001 Office Action is due October 11, 2001. Accordingly, this Amendment is being timely filed.

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Please amend the subject application as follows:

In the claims:

Please amend claim 1 as follows:

-- 1. (Amended) A method of treating urinary incontinence in a subject which comprises administering to a subject suffering from urinary incontinence a therapeutically effective amount of a 5-HT_{1F} receptor agonist which activates the human 5-HT_{1F} receptor at least ten-fold more than it activates each of the human 5-HT_{1A}, 5-HT_{1D}, 5-HT_{2A}, 5-HT_{2C}, 5-HT_3, 5-HT_4, and 5-HT_7 receptors.--

A1
B1

A marked-up version of amended claim 1 showing the changes made is attached hereto as **Exhibit A**.

REMARKS

Claims 1-24 were pending in the subject application. By this Amendment applicant has amended claim 1. Accordingly, upon entry of this Amendment, claims 1-24 as amended will be pending and under examination.

Applicant maintains that the amendment to claims 1 does not raise any issue of new matter and that this claim is fully supported by the specification as filed. Support for the amendment to claim 1 may be found inter alia in the specification as originally filed on page 13, lines 13-14.

Accordingly, applicant respectfully requests that the Amendment be entered.

Rejection under 35 U.S.C. §112, first paragraph

On page 2 of the April 11, 2001 Office Action, the Examiner rejected claims 1-24 under 35 U.S.C. §112, first paragraph, allegedly because the specification, while being enabling for known 5-HT_{1F} agonists and analogs with similar structures, does not reasonably provide enablement for the generic class of 5-HT_{1F} agonists defined only by the desired property of specific activation of the 5-HT_{1F} receptor. The Examiner alleged that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The Examiner stated that claims 1-24 are broadly drawn to 5-HT_{1F} agonists which specifically activate only the 5-HT_{1F} receptor and that these claims recite activation of 5-HT_{1F} to various levels higher than other receptors, such as other 5-HT receptors, "adrenoceptors" and histamine receptors. The Examiner alleged that the specification, however, lacks guidance on how to make, de novo, any receptor agonists that would have these properties and that the specification merely refers to previously isolated and tested agonists. See, for example specification page 17, lines 10-32. The Examiner alleged that the molecular structure of these agonists are unpredictable and that given the core ring structure of an agonists, one could not predict any of the other core ring structures.

The Examiner further stated that the prior art disclosures of agonists lack any general guidance that would direct one to systematically make a reasonable number of agonists having the claimed properties. See for example Flaugh et al., United States Patent 5,846,995, 12/1998. The Examiner stated that Flaugh et al. disclose agonists without any guidance on how these particular structures were chosen and that Flaugh et al. simply demonstrate that their agonists function by testing the agonists in various binding assays. See Flaugh et al. col. 42, Table II, for example. The Examiner thus alleged that the state of the art in this field is that one can predict only the generally applicable organic chemistry rule that molecules having analagous structure will have similar properties and one cannot predict, using the ring structure of one class of agonists, the structure of a new, distinct class of agonists.

The Examiner concluded that due to the great breadth of the claims, the lack of guidance in the current specification and the unpredictability of finding new classes of agonists, it would require undue experimentation for the art skilled to enable a reasonable number of embodiments and that the art skilled would be forced to perform brute force trial and error of making arbitrarily chosen compounds and testing them in binding assays without any guidance on which compounds would function.

In response, applicant traverses the Examiner's rejection for the following reasons. The claims are directed to methods of treating urinary incontinence which comprise administering a selective 5-HT_{1F} receptor agonist to a subject suffering from

urinary incontinence. The subject application provides examples of selective 5-HT_{1F} receptor agonists on page 17, lines 9-21; page 22, lines 21-23; and Table 1 on page 25. The greater binding affinity of these agonists for the 5-HT_{1F} receptor as compared to other serotonin receptor subtypes is described in Table 1.

In addition, selective 5-HT_{1F} receptor agonists are well known to those skilled in the art, as evidenced for example by the 13 United States patents cited in the specification on page 17, lines 25-31, the disclosures of which are incorporated by reference into the subject application. Copies of these 13 patents are attached hereto as **Exhibits 1-13** as follows: U.S. Patent Nos. 5,521,196 (Exhibit 1), 5,521,197 (Exhibit 2), 5,708,187 (Exhibit 3), 5,792,763 (Exhibit 4), 5,814,653 (Exhibit 5), 5,817,671 (Exhibit 6), 5,846,995 (Exhibit 7), 5,905,084 (Exhibit 8), 5,708,008 (Exhibit 9), 5,721,252 (Exhibit 10), 5,814,653 (Exhibit 11), 5,919,936 (Exhibit 12), and 5,874,427 (Exhibit 13). These 13 patents identify numerous 5-HT_{1F} receptor agonists. As examples, U.S. Patent No. 5,5521,196 (Exhibit 1) lists 55 5-HT_{1F} receptor agonists (column 11, line 29 through column 23, line 28; TABLE I); U.S. Patent No. 5,521,197 (Exhibit 2) lists 48 5-HT_{1F} receptor agonists (column 11, line 48 through column 22, line 60; TABLE I); and U.S. Patent No. 5,708,187 (Exhibit 3) lists 115 5-HT_{1F} receptor agonists (column 37, line 10 through column 68, line 53; column 69, lines 37-39). Furthermore, the binding affinities of five 5-HT_{1F} receptor agonists are characterized at multiple serotonin receptor subtypes (see e.g. U.S. Patent No. 5,521,196 (Exhibit 1), TABLE II; column 26, line 25 through column 29, line 60).

Methods for determining the relative binding affinities of a compound at different receptor subtypes are well known in the art. Descriptions of these methods can be found in the subject application on page 20, line 15 through page 22, line 17, and in the specifications of the 13 United States Patents attached hereto as Exhibits 1-13. Applicant maintains that it is a routine matter, not requiring undue experimentation, to characterize the binding profile of a 5-HT_{1F} receptor agonist at other receptor subtypes and thus it would be a routine matter to identify 5-HT_{1F} receptor agonists which meet the criteria of the subject claims.

Accordingly, applicant maintains that the teachings of the specification enable the skilled artisan to practice the subject invention.

Applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection in view of the remarks made herein above.

Rejection under 35 U.S.C. §102(a)

On page 3 of the April 11, 2001 Office Action, the Examiner rejected claims 1-24 under 35 U.S.C. §102(a) as allegedly being anticipated by Flaugh et al., United States Patent No. 5,846,995, 12/1998.

The Examiner stated that the treatment claims of the current case are broadly drawn to "administering" a "therapeutically effective amount" of an agonist and that the agonist is not limited to any structure but merely limited by recited

characteristics of an agonist which specifically activates the 5-HT_{1F} receptor rather than various other receptors.

The Examiner alleged that these claims read on the Flaugh et al. treatment methods. The Examiner stated that Flaugh discloses "administering" therapeutically effective amounts of a 5-HT_{1F} agonists (col. 2, lines 28-33; col. 29, lines 40-52).

The Examiner noted that while the claim preamble of the subject application recites "treating urinary incontinence", the Examiner alleged that there is no positive method step which limits the claim to avoid the Flaugh treatments. Thus, the Examiner concluded that the claims cover both incontinence treatment and Flaugh's migraine headache treatment.

The Examiner suggested that the claims be limited, for example by adding a step reciting "administering to a patient suffering from urinary incontinence". The Examiner indicated that support for any amendment (even those suggested by Examiners) must be pointed out in the original disclosure.

Applicant thanks the Examiner for the suggested amendment to the claims.

In response, in an attempt to advance the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicant has amended claim 1 to recite:

> A method of treating urinary incontinence in a subject which comprises administering to a subject

> suffering from urinary incontinence a therapeutically effective amount of a 5-HT_{1F} receptor agonist which activates the human 5-HT_{1F} receptor at least ten-fold more than it activates each of the human 5-HT_{1A}, 5-HT_{1D}, 5-HT_{2A}, 5-HT_{2C}, 5-HT_3, 5-HT_4, and 5-HT_7 receptors.

Claims 2-24 depend from claim 1. Applicant maintains that claims 1-24, as amended, are not anticipated by Flaugh et al., United States Patent No. 5,846,995, 12/1998, since Flaugh et al. do not teach or suggest administering a 5-HT_{1F} receptor agonist to a subject suffering from urinary incontinence in order to treat the subject's urinary incontinence.

Applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection in light of the aforementioned amendment and remarks.

In summary, in light of the remarks and amendments made hereinabove, applicant respectfully request that the Examiner reconsider and withdraw the various grounds of rejection set forth in the April 11, 2001 Office Action and earnestly solicits allowance of the claims now pending in the subject application, namely claims 1-24.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $920.00 fee for a three month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if an additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

10/4/01

John P. White Date
Reg. No. 28,678